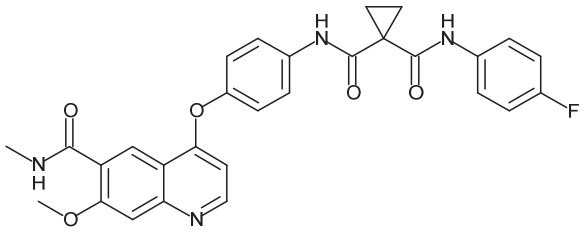
receptor. Tumor cells secrete a soluble form of the extracellular Mer receptor which reduces the ability of soluble Gas-6 ligand to activate Mer on endothelial cells, leading to cancer progression.

[0005] Therefore a need exists for compounds that inhibit TAM receptor tyrosine kinases such as Axl and Mer for the treatment of selected cancers.

Summary of the Disclosure

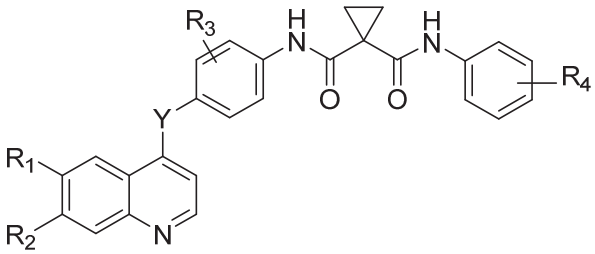
[0005a] In one aspect, provided herein is a compound which is:



or a pharmaceutically acceptable salt thereof.

[0005b] In one aspect, provided herein is a compound which is 1-N'-(4-fluorophenyl)-1-N-[4-[7-methoxy-6-(methylcarbamoyl)quinolin-4-yl]oxyphenyl]cyclopropane-1,1-dicarboxamide or a pharmaceutically acceptable salt thereof.

[0006] In one example, the present disclosure provides a compound of formula I:



I

or a pharmaceutically acceptable salt thereof, wherein:

R_1 is selected from the group consisting of -H, -CN, -CO-NR_5R_6, -CO_2R_7, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted (C_1-C_6) alkyl, optionally substituted (C_3-C_8) cycloalkyl, optionally substituted (C_3-C_6) heterocycloalkyl, -$SO_2NR_8R_9$, and -(SO_2)-(C_1-C_6) alkyl;

wherein when R_1 is selected from the group consisting of -CN, -CO-NR_5R_6, -CO_2R_7, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted (C_3-C_8) cycloalkyl, optionally substituted (C_3-C_6) heterocycloalkyl, -$SO_2NR_8R_9$, and -(SO_2)-(C_1-C_6) alkyl, R_2 is -H, halo, -NR_5R_6, or optionally substituted (C_1-C_6) alkoxy;

wherein when R_1 is -H, optionally substituted (C_1-C_6) alkyl, or optionally substituted (C_1-C_6) alkoxy, R_2 is -CO-NR_5R_6; or -CO_2R_7;

or R_1 and R_2 taken together with the atoms to which they are attached to form optionally substituted cycloalkyl or optionally substituted heterocyloalkyl;

R_3 is selected from the group consisting of -H, optionally substituted (C_1.C_6) alkyl, -CN, and halo;

R_4 is -H or halo;

 is optionally substituted with one, two, three, or four groups independently selected from the group consisting of halo and (C_1-C_6) alkyl, wherein "〰" indicate points of attachment;

R_5 and R_6 are each independently -H, optionally substituted (C_1-C_6) alkyl, or optionally substituted (C_1-C_6) alkoxy;

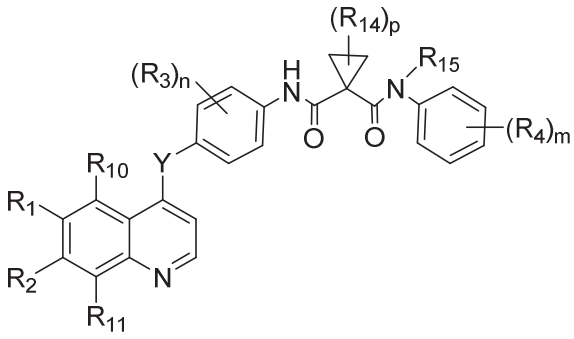
R_7 is -H or optionally substituted (C_1-C_6) alkyl

R_8 and R_9 are each independently -H or optionally substituted (C_1-C_6) alkyl;

or R_8 and R_9 may connect to form an optionally substituted heterocycle; and

Y is selected from the group consisting of O, S, SO, SO_2, NH, and N-(C_1-C_6 alkyl).

[0007] Another example provides a compound of formula A:



A

or a pharmaceutically acceptable salt thereof, wherein

(i) R_1 is selected from the group consisting of (C_2-C_6) alkenyl, (C_2-C_6) alkynyl, (C_6-C_{10}) aryl, (C_3-C_{10}) cycloalkyl, 5-10 membered heteroaryl, 4-10 membered heterocycloalkyl, -CN,-NHOH, -C(O)R^a, -C(O)NR^aR^a, -C(O)NHOR^a, -C(O)OR^a, -C(O)$NR^aS(O)_2R^a$, -OC(O)NR^aR^a, C(=NR^a)R^a, -C(=NOH)R^a, -C(=NOH)NR^a, -C(=NCN)NR^aR^a, -C(=NR^a)NR^aR^a, -S(O)NR^aR^a, -$S(O)_2NR^aC(O)R^a$, -P(O)R^aR^a, -P(O)(OR^a)(OR^a), -$B(OH)_2$, -$B(OR^a)_2$, and $S(O)_2NR^aR^a$; and

R_2 is selected from -H, halo, (C_1-C_6) alkyl, (C_2-C_6) alkenyl, (C_2-C_6) alkynyl, (C_1-C_6) haloalkyl, (C_1-C_6) haloalkoxy, (C_6-C_{10}) aryl-(C_1-C_4) alkylene-, (C_3-C_{10}) cycloalkyl-(C_1-C_4) alkylene-, (5-14 membered heteroaryl)-(C_1-C_4) alkylene-, (4-14 membered heterocycloalkyl)-(C_1-C_4) alkylene-, -CN, -NO_2, -OR^a, -SR^a, -NHOR^a, -C(O)R^a, -C(O)NR^aR^a, -C(O)NHOR^a, -C(O)OR^a, -C(O)$NR^aS(O)_2R^a$, -OC(O)R^a, -OC(O)NR^aR^a, -NHR^a, -NR^aR^a, -$NR^aC(O)R^a$, -$NR^aC(=NR^a)R^a$, -$NR^aC(O)OR^a$, -$NR^aC(O)NR^aR^a$, -C(=NR^a)R^a, -C(=NOH)R^a, -C(=NOH)NR^a, -C(=NCN)NR^aR^a, -$NR^aC(=NCN)NR^aR^a$, -C(=NR^a)NR^aR^a, -$NR^aC(=NR^a)NR^aR^a$, -$NR^aS(O)R^a$, -

each R^g is independently selected from the group consisting of halo, -OH, -CN, -COOH, -COO-(C_1-C_4) alkyl, -NH_2, -NH-(C_1-C_6) alkyl, -N((C_1-C_6) alky)$_2$, (C_1-C_6) alkyl, (C_1-C_6) alkoxy, (C_1-C_6) alkylthio, (C_1-C_6) haloalkyl, (C_1-C_6) haloalkoxy, phenyl, 5-6 membered heteroaryl, 4-6 membered heterocycloalkyl, and (C_3-C_6) cycloalkyl;

Y is selected from -O-, -S-, -SO-, -SO_2-, -NH-, and –N((C_1-C_6) alkyl)-;

the ring nitrogen atom on the quinoline moiety in Formula A is optionally oxidized;

the subscript n is an integer of 1, 2, 3, or 4;

the subscript m is an integer of 1, 2, 3, 4, or 5; and

the subscript p is an integer of 0, 1, 2, 3, or 4.

[0008] Another example provides methods of using compounds of formula I or a pharmaceutically acceptable salt thereof for the treatment of a disease, disorder, or syndrome mediated at least in part by modulating in vivo activity of a protein kinase.

[0009] A further example provides processes for making compounds of formula A and of formula I.

[00010] These and other examples are described below.

Detailed Description of the Invention

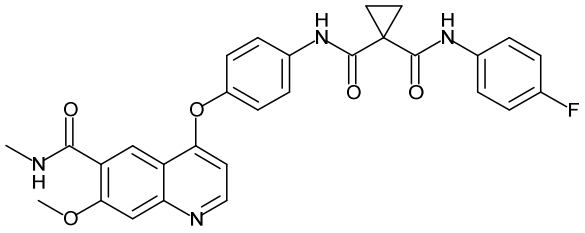
Abbreviations and Definitions

[00011] The following abbreviations and terms have the indicated meanings throughout:

Abbreviation	Meaning
Ac	Acetyl
anhyd	Anhydrous
Aq	Aqueous
Ar	Argon
Boc	Tert-butoxycarbonyl
Br	Broad
°C	Degrees Celsius
c-	Cyclo
calcd	Calculated
CBZ	CarboBenZoxy = benzyloxycarbonyl
d	Doublet
dd	Doublet of doublets
ddd	Doublet of doublets of doublets
dt	Doublet of triplets
DCM	Dichloromethane

Claims

1. A compound which is:



or a pharmaceutically acceptable salt thereof.

2. A compound which is 1-N'-(4-fluorophenyl)-1-N-[4-[7-methoxy-6-(methylcarbamoyl)quinolin-4-yl]oxyphenyl]cyclopropane-1,1-dicarboxamide or a pharmaceutically acceptable salt thereof.